

IN THE CLAIMS

Please amend claims 9 and 11 and add claims 13-16 as follows:

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1. (WITHDRAWN) An aqueous insulin formulation comprising insulin, a buffer system, an isotonicity agent, a preservative, metal ions, and a non-ionic surfactant selected from at least a polysorbate, a poloxyethylene ether, a polyethylene glycol ether, and mixtures of these surfactants.
  2. (WITHDRAWN) The aqueous insulin formulation of claim 1, wherein the insulin is human insulin.
  3. (WITHDRAWN) The aqueous insulin formulation of claim 2, wherein the human insulin is a recombinant insulin.
  4. (WITHDRAWN) The aqueous insulin formulation, wherein the preservative is selected from at least phenol, m-cresol and mixture of these preservatives.
  5. (WITHDRAWN) An aqueous insulin formulation comprising insulin, a buffer system, an isotonicity agent, a preservative, metal ions and a non-ionic surfactant selected from at least a polysorbate, a poloxyethylene ether, a polyethylene glycol, and mixtures of these surfactants, wherein the insulin formulation exhibits a physical stability that is greater than or equal to the same insulin formulation containing the non-ionic surfactant Genapol PF-10.
  6. (WITHDRAWN) The aqueous insulin formulation of claim 1, wherein the insulin concentration is about 2 U/ml to about 1000 U/ml.
  7. (WITHDRAWN) The aqueous insulin formulation of claim 6, wherein the insulin concentration is about 400 U/ml.
  8. (WITHDRAWN) An insulin infusion device comprising:  
an insulin pump system; and

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a surfactant-stabilized insulin formulation including insulin and a non-ionic surfactant selected from at least a polysorbate, a poloxyethylene ether, a polyethylene glycol ether, and mixtures of these surfactants.

9. (CURRENTLY AMENDED) A method of evaluating the physical stability of a protein formulation comprising:

(a) preparing a statistically relevant number of identical samples of a protein formulation to yield a first sample type, wherein the protein is susceptible to changes in its native conformation yielding non-native conformers of the protein;

(b) preparing a statistically relevant number of identical samples of at least one other protein formulation that differs from the first sample type to yield a second, or more, sample types, wherein the protein is susceptible to a changes in its native conformation yielding non-native conformers of the protein;

~~adding an agent that yields a change upon binding to a non-native conformer of the protein;~~  
wherein the samples prepared in steps (a) and (b) further comprise an agent that produces an observable signal when bound to a non-native conformer of the protein;

(c) applying a controlled stress on all sample types, wherein the controlled stress applied causes the protein to exhibit a change in its native conformation;

(d) monitoring the observable signal produced by the agent in the samples types to yield time-dependent data that are related to a degree of protein conformational change for each sample type;

(e) applying a survival analysis to the data obtained for each sample type; and

(f) comparing the survival analysis for each sample type to determine the relative physical stability of the protein formulations under evaluation.

10. (ORIGINAL) The method of claim 9, wherein the controlled stress is agitation.

11. (CURRENTLY AMENDED) The method of claim 9, wherein the ~~spectroscopic change is a spectroscopic change in fluorescence~~ observable signal is a fluorescent signal.

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12. (ORIGINAL) The method of claim 9, wherein the protein is insulin and the non-native conformer of the protein is a fibril form of insulin.

13. (NEW) The method of claim 9, wherein the protein formulation comprises an insulin analogue.

14. (NEW) The method of claim 9, wherein the agent that produces an observable signal when bound to a non-native conformer of the protein is Thioflavin-T.

15. (NEW) The method of claim 9, wherein the sample volume of the protein formulations of steps (a) and (b) are from about 1  $\mu$ l to about 1000  $\mu$ l.

16. (NEW) The method of claim 15, wherein the sample volume of the protein formulations of steps (a) and (b) are from about 50  $\mu$ l to about 500  $\mu$ l.

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